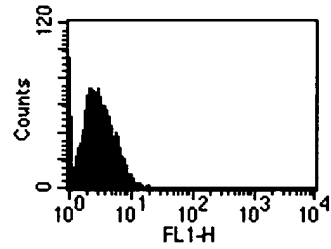


FIGURE 1

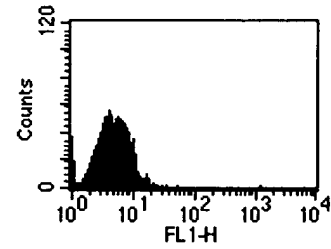
Y1251F IGF-I Receptor Cells

Insulin Receptor Cells

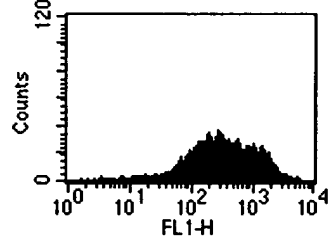
Goat $\alpha$ mouse-IgG-FITC only



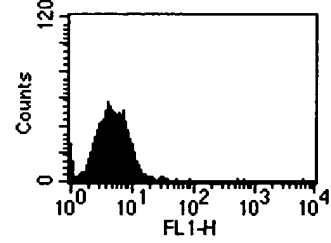
Goat $\alpha$ mouse-IgG-FITC only



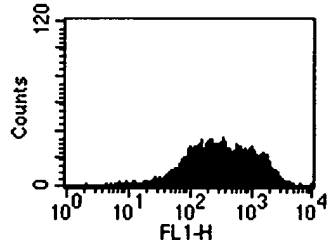
100 nM  $\alpha$ EM164



100 nM  $\alpha$ EM164



100 nM  $\alpha$ 1H7



100 nM  $\alpha$ IR

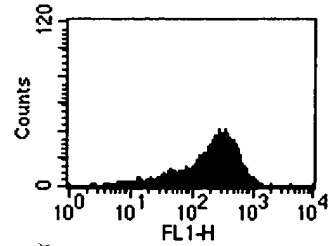


FIGURE 2

**Titration curve for binding  
of EM164 antibody to  
biotinylated IGF-I Receptor**

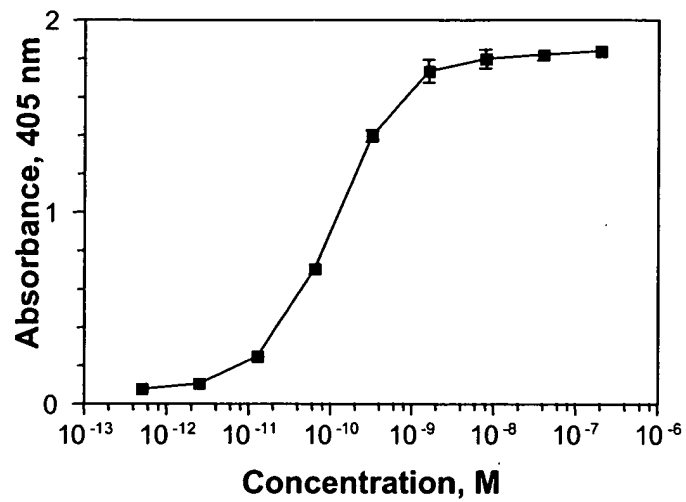


FIGURE 3

**Inhibition of binding of biotin-IGF-I  
to MCF-7 Cells by EM164 antibody**

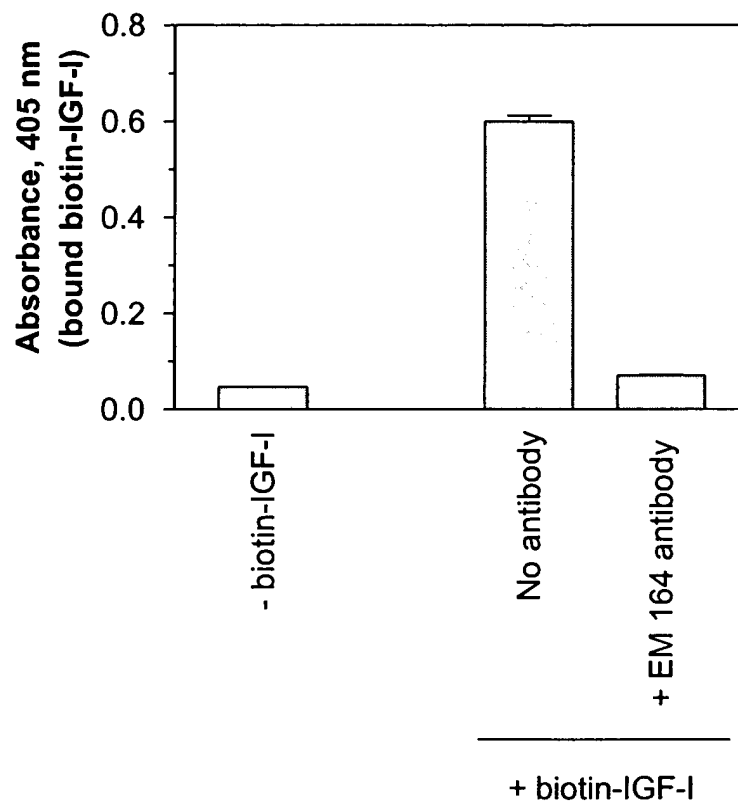


FIGURE 4

**Inhibition of IGF-I-Stimulated Autophosphorylation of IGF-I Receptor in MCF-7 Cells by EM164 Antibody**

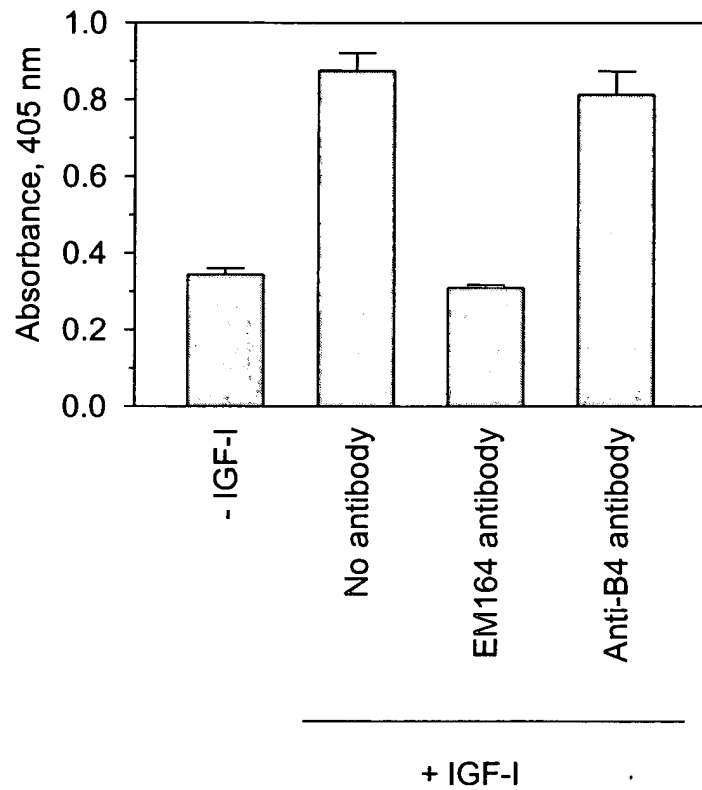


FIGURE 5

**Inhibition of IGF-I-Stimulated IRS-1-Phosphorylation  
 in MCF-7 Cells by EM 164 antibody**

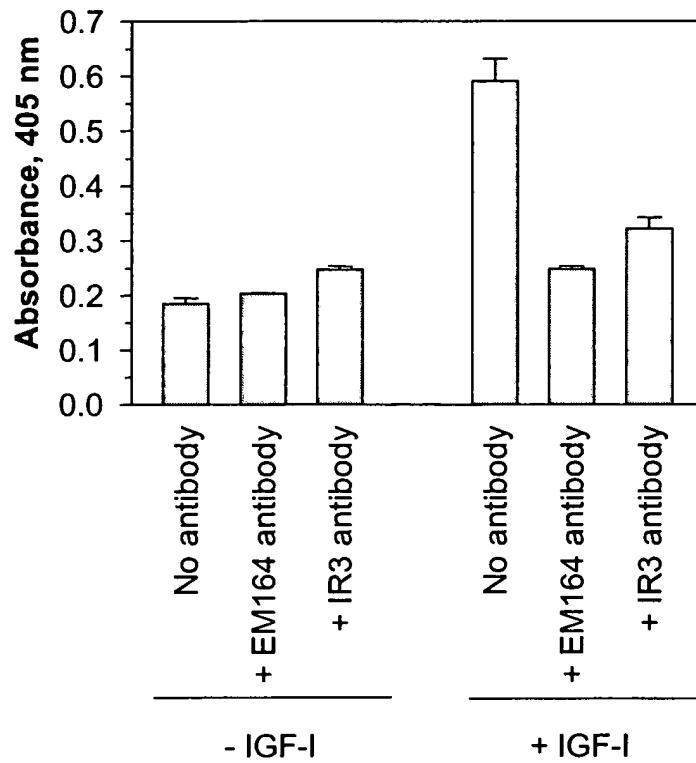


FIGURE 6

**Inhibition of IGF-I-Stimulated Signal Transduction  
 in SaOS-2 Cells by EM164 Antibody**

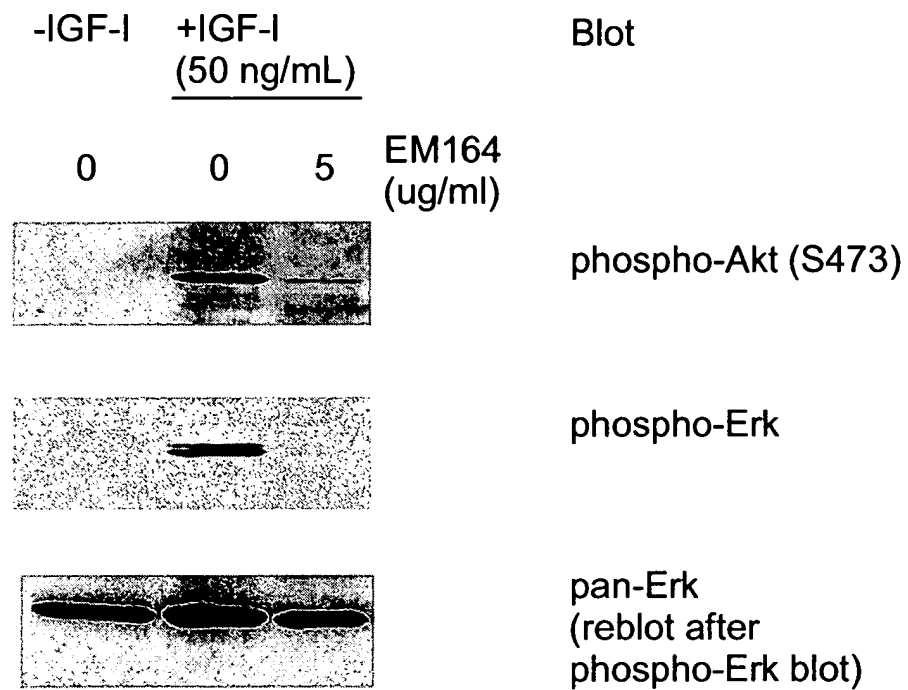


FIGURE 7

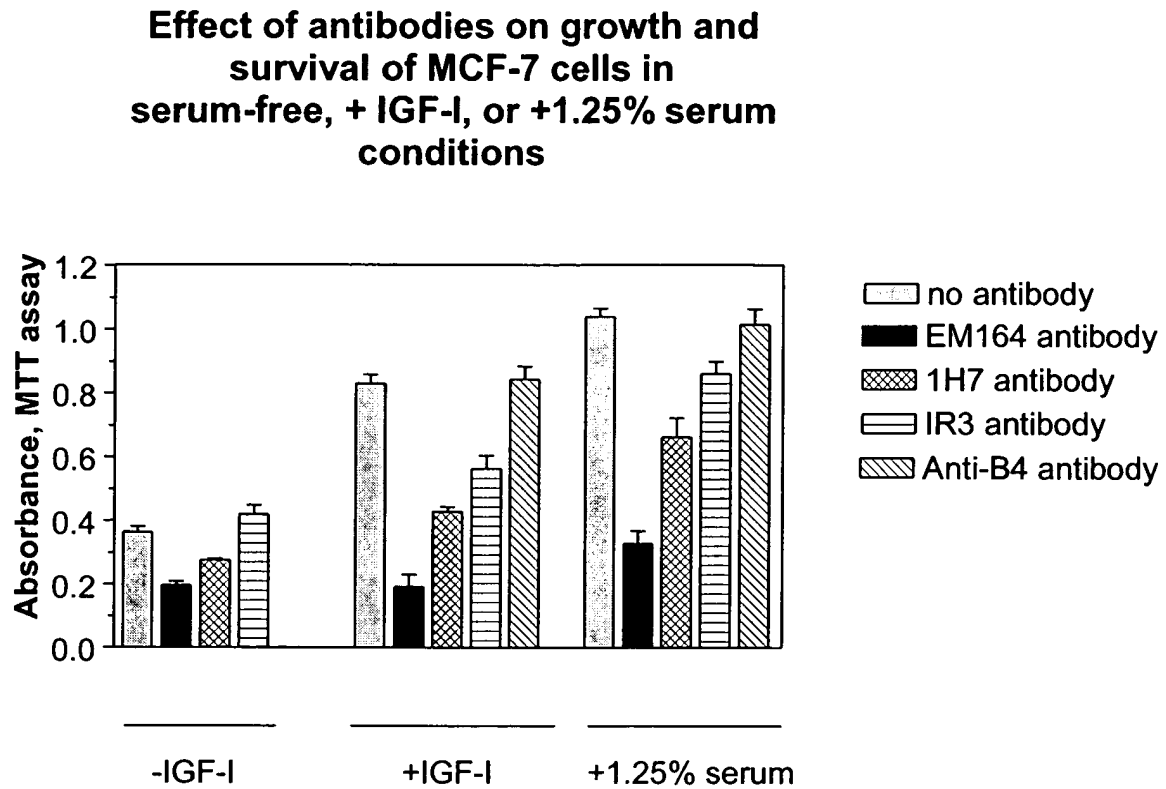


FIGURE 8

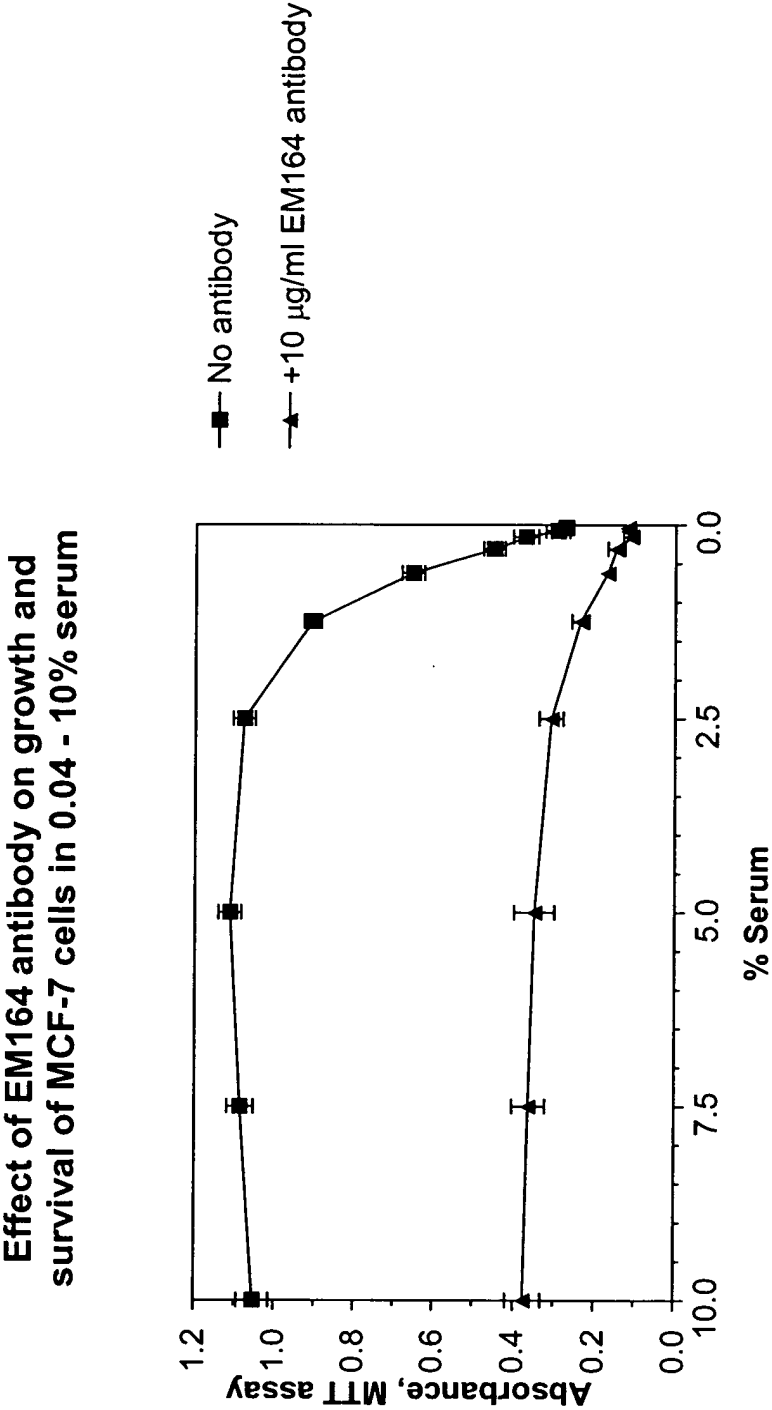




FIGURE 9

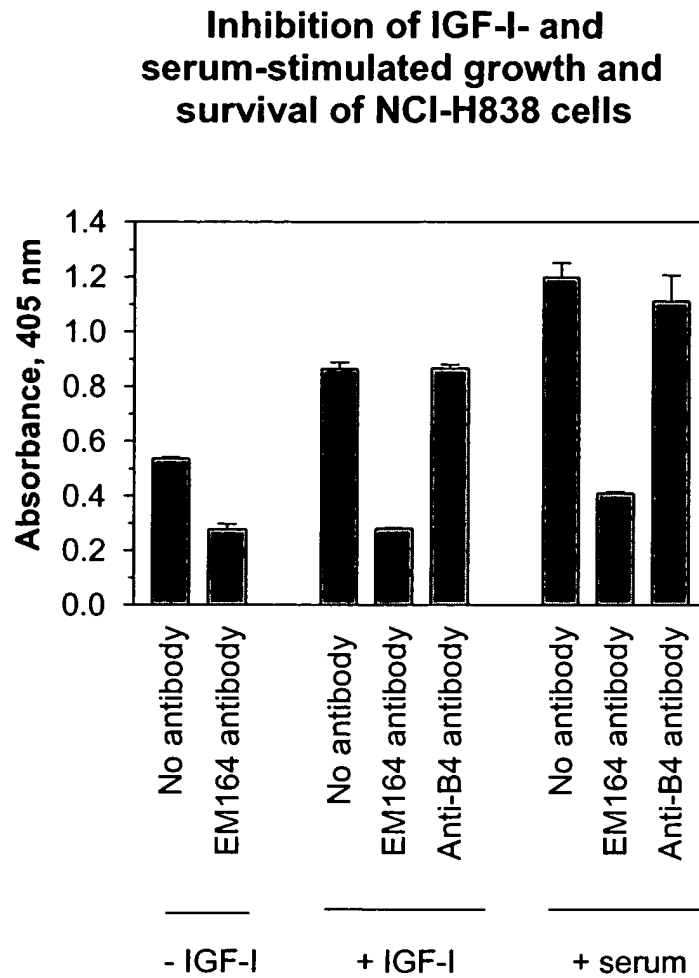


FIGURE 10

**Effect of treatment with EM164 antibody, or taxol, or a combination of EM164 antibody and taxol, on growth of Calu-6 lung cancer xenograft in mice**

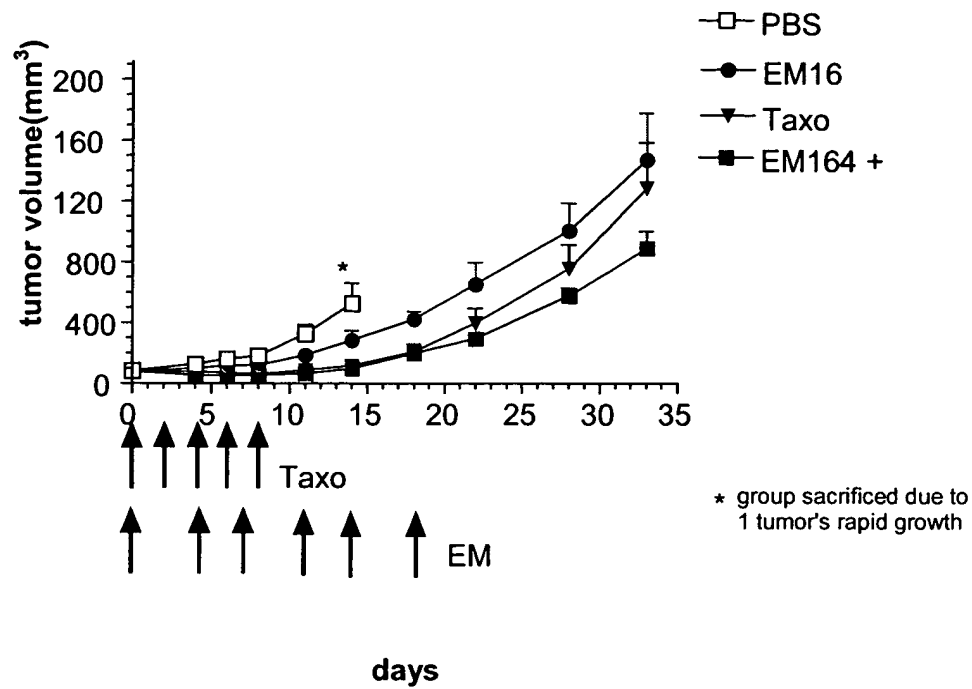


FIGURE 11

**Competition of binding of humanized EM164 antibody (version 1.0) to immobilized biotinylated IGF-I receptor by murine EM164 antibody (1.06 to 10.6-fold molar concentration range)**

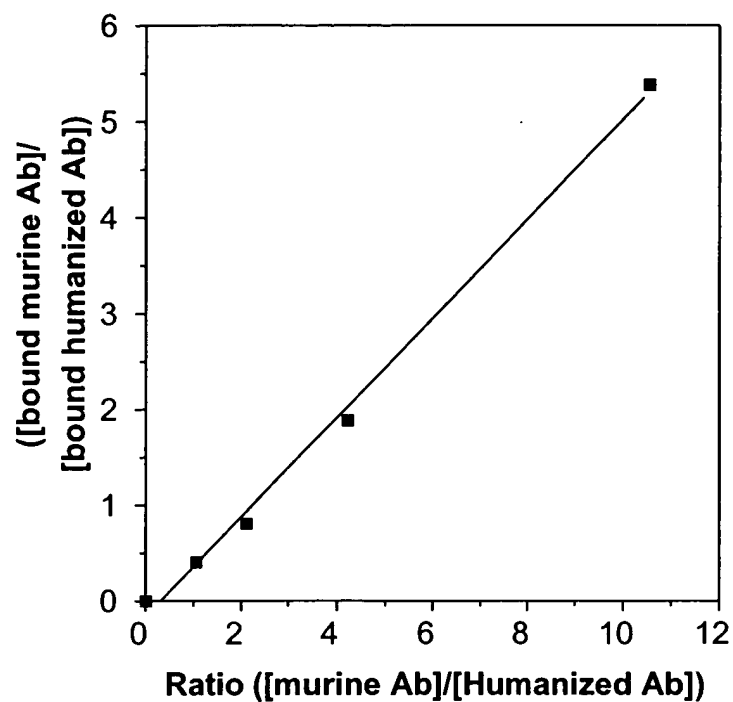


FIGURE 12

→  
**Murine EM164 Light Chain**

```

1 atgaagttgcctgttaggctggttggtgctgatgttctggattcct
1 M K L P V R L L V L M F W I P

46 gcttccagtagtgatggtttgatgacccaaactccactctccctg
16 A S S S D V L M T Q T P L S L
   -VK

91 cctgtcagtccttgagatcaagcctccatctcttgagatctagt
31 P V S L G D Q A S I S C R S S
                               CDR1

136 cagagcattgtacatagtaatgtaaacacctatttagaattggtac
46 Q S I V H S N V N T Y L E W Y
      CDR1

181 ctgcagaaaccaggccagtcctcaaagctcctgatctacaaagtt
61 L Q K P G Q S P K L L I Y K V
                               CDR2

226 tccaaccgattttctgggggtcccagacaggttcagtggcagtgga
76 S N R F S G V P D R F S G S G
      CDR2

271 tcagggacagatttcacactcaggatcagcagagtggaggctgag
91 S G T D F T L R I S R V E A E

316 gatctgggaattttattactgctttcaagggttcacatgttcctccg
106 D L G I Y Y C F Q G S H V P P
                               CDR3

361 acgttcggtggaggcaccaagctggaaatcaaacgg
121 T F G G G T K L E I K R

```

FIGURE 13

→  
**Murine EM164 Heavy Chain**

```

1 atgggatggagctatatcatcctctttttggtagcaacagctaca
1  M G W S Y I I L F L V A T A T

46 gaagtcactcccaggtccaactgcagcagtcctggggctgaactg
16  E V H S Q V Q L Q Q S G A E L
    -VH

91 gtgaagcctggggcttcagtgaagctgtcctgtaaggcttctggc
31  V K P G A S V K L S C K A S G

136 tacaccttcaccagctactggatgcactgggtgaagcagaggcct
46  Y T F T S Y W M H W V K Q R P
           CDR1

181 ggacaaggccttgagtggattggagagattaatcctagcaacggt
61  G Q G L E W I G E I N P S N G
                        CDR2

226 cgtactaactacaatgagaagttcaagaggaaggccacactgact
76  R T N Y N E K F K R K A T L T
           CDR2

271 gtagacaaatcctccagcacagcctacatgcaactcagcagcctg
91  V D K S S S T A Y M Q L S S L

316 acatctgaggactctgcggtctattactttgcaagaggaagacca
106 T S E D S A V Y Y F A R G R P
                                CDR3

361 gattactacggtagtagcaagtggtagtctcgatgtctggggcgca
121 D Y Y G S S K W Y F D V W G A
           CDR3

406 gggaccacgggtcaccgtctcctca
136 G T T V T V S S

```

FIGURE 14

**Murine EM164 CDRs**

**Light Chain**

CDR1: R S S Q S I V H S N V N T Y L E

CDR2: K V S N R F S

CDR3: F Q G S H V P P T

**Heavy Chain**

CDR1: S Y W M H

CDR2: E I N P S N G R T N Y N E K F K R

CDR3: G R P D Y Y G S S K W Y F D V

**AbM Heavy Chain**

CDR1: G Y T F T S Y W M H

CDR2: E I N P S N G R T N

CDR3: G R P D Y Y G S S K W Y F D V

FIGURE 15

**Germline sequence comparisons**

<b>Light Chain</b>		<b>50</b>
Cr1	- DVLMTQTPLSLPVSLGDQASISCRSSQSI VHSNGNTYLEWYLQKPGQSPK	
muEM164	- -----V-----	
		<b>100</b>
Cr1	- LLIYKVSNRFSGV PDRFSGSGGTDFTLKISRVEAEDLGVIYCFQGSHVP	
muEM164	- -----R-----I-----	
<b>Heavy Chain</b>		<b>50</b>
J558.c	- QVQLQQPGAELVKPGASVKLSCKASGYTFTSYWMHWVKQRPGQGLEWIGE	
muEM164	- -----S-----	
		<b>98</b>
J558.c	- INPSNGRTNYNEKFKSKATLTVDKSSSTAYMQLSSPTSEDSAVYYCAR	
muEM164	- -----R-----L-----F--	

FIGURE 16

# Cloning and Mammalian Expression Plasmid Maps

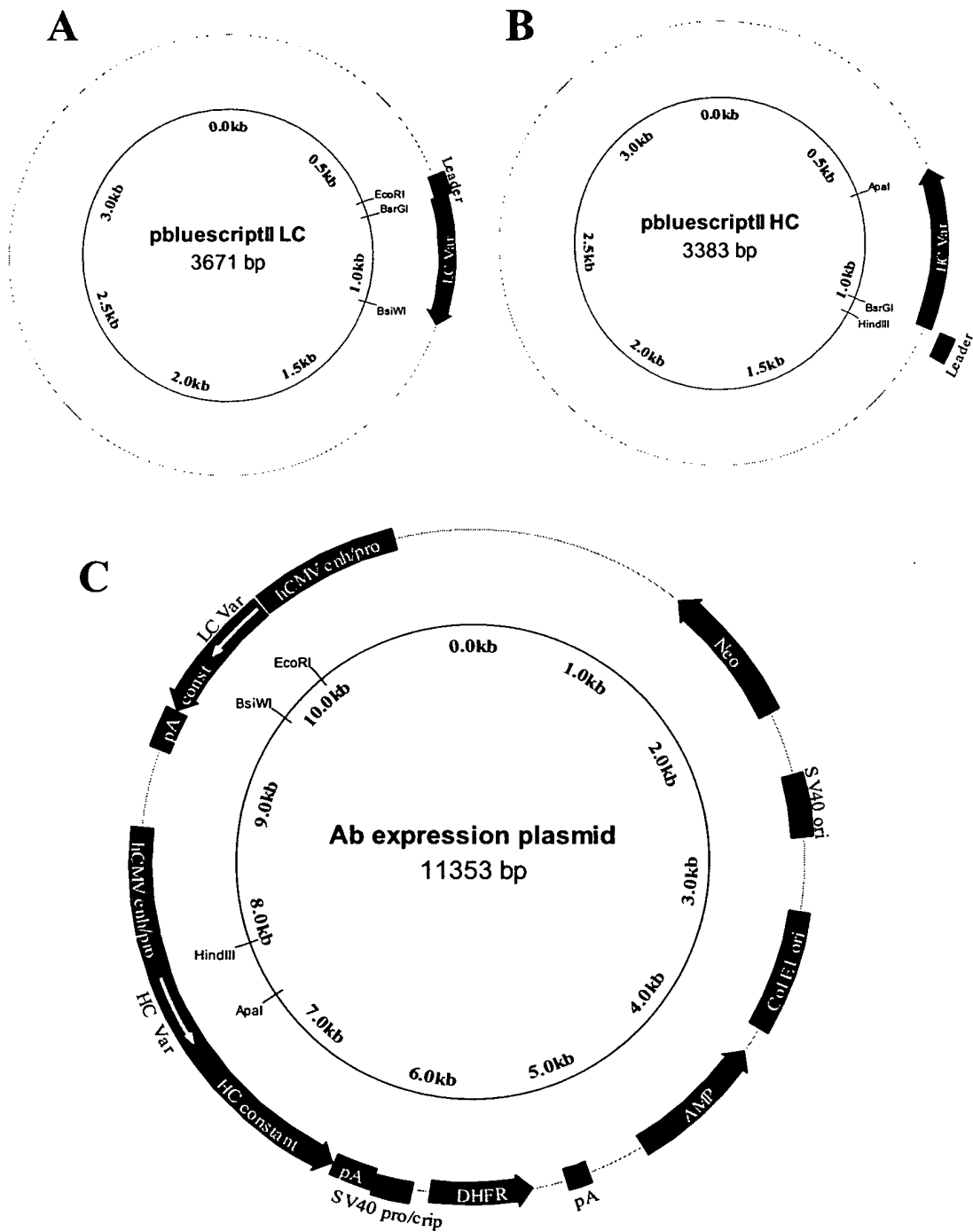




FIGURE 17

# 10 Most Homologous Light Chain Sequence Alignment

	1	10	20	30	40	50
em164 LC	DVLM	TQTPLS	LPVSLGDQAS	ISCRSSQSIV	HSNVNTYLEW	YLQKPGQSPK
2jel	DVLM	TQTPLS	LPVSLGDQAS	ISCRSSQSIV	HSNGNTYLEW	YLQKPGQSPK
2pcp	DVLM	TQTPLS	LPVSLGDQAS	ISCRSSQSIV	HSNGNTYLEW	YLQKPGQSPK
lnqb	DIEL	TQTPLS	LPVSLGDQAS	ISCRSSQSIV	HSNGNTYLEW	YLQKPGQSPK
lkel	DVLM	TQTPLS	LPVSLGDQAS	ISCRSSQSIV	HSNGNTYLEW	YLQKPGQSPK
lhyx	ELVM	TQTPLS	LPVSLGDQAS	ISCRSSQSIV	HSNGDITYLEW	FLQKPGQSPK
ligf	DVLM	TQTPLS	LPVSLGDQAS	ISCRSSQSIV	HSNGDITYLEW	YLQKPGQSPK
ltet	DVLM	TQTPLS	LPVSLGDQAS	ISCRSSQSIV	HSNGDITYLEW	YLQKPGQSPK
lclz	DVLM	TQTPLS	LPVSLGDQAS	ISCRSSQSIV	HSNGDITYLEW	YLQKPGQSPK
lbln	DVLM	TQTPLS	LPVSLGDQAS	ISCRSSQSIV	HSNGDITYLEW	YLQKPGQSPK
lcly	DVLM	TQTPLS	LPVSLGDQAS	ISCRSSQSIV	HSNGDITYLEW	YLQKPGQSPK
Consensus	d v l m T Q T P L S	L p V S L G D Q A S	I S C R s s Q x I v	h s n g n t Y l e W	y L Q K p G Q S P k	

	60	70	80	90	100	
em164 LC	LLIYKVS	NRFSGVPDRFSGS	GSGTDFTLKI	SRVEAEDLG	VYYCFQGS	HVP
2jel	LLIYKVS	NRFSGVPDRFSGS	GSGTDFTLKI	SRVEAEDLG	VYYCFQGS	HVP
2pcp	LLIYKVS	NRFSGVPDRFSGS	GSGTDFTLKI	SRVEAEDLG	VYYCFQGS	HVP
lnqb	LLIYKVS	NRFSGVPDRFSGS	GSGTDFTLKI	SRVEAEDLG	VYYCFQGS	HVP
lkel	LLIYKVS	NRFSGVPDRFSGS	GSGTDFTLKI	SRVEAEDLG	VYYCFQGS	HVP
lhyx	LLIYKVS	NRFSGVPDRFSGS	GSGTDFTLKI	SRVEAEDLG	VYYCFQGS	HVP
ligf	LLIYKVS	NRFSGVPDRFSGS	GSGTDFTLKI	SRVEAEDLG	VYYCFQGS	HVP
ltet	LLIYKVS	NRFSGVPDRFSGS	GSGTDFTLKI	SRVEAEDLG	VYYCFQGS	HVP
lclz	LLIYKVS	NRFSGVPDRFSGS	GSGTDFTLKI	SRVEAEDLG	VYYCFQGS	HVP
lbln	LLIYKVS	NRFSGVPDRFSGS	GSGTDFTLKI	SRVEAEDLG	VYYCFQGS	HVP
lcly	LLIYKVS	NRFSGVPDRFSGS	GSGTDFTLKI	SRVEAEDLG	VYYCFQGS	HVP
Consensus	L L I Y k v s n r f	S G V P D R F S G S	G S G T D F T L k I	S R V e A E D L G v	Y Y C F Q g s H v P	

	110	120	130	140	150
em164 LC	PTFGG	GGTKLE	IKR		
2jel	YTFGG	GGTKLE	IKR		
2pcp	YTFGG	GGTKLE	IKR		
lnqb	YTFGG	GGTKLE	IKR		
lkel	RTFGG	GGTKLE	IKR		
lhyx	PTFGG	GGTKLE	IKR		
ligf	PTFGG	GGTKLE	IKR		
ltet	FTFGS	GGTKLE	IKR		
lclz	FTFGS	GGTKLE	IKR		
lbln	RTFGG	GGTKLE	IKR		
lcly	FTFGS	GGTKLE	IKR		
Consensus	x T F G g G T K L E	I K R			

FIGURE 18

# 10 Most Homologous Heavy Chain Sequence Alignment

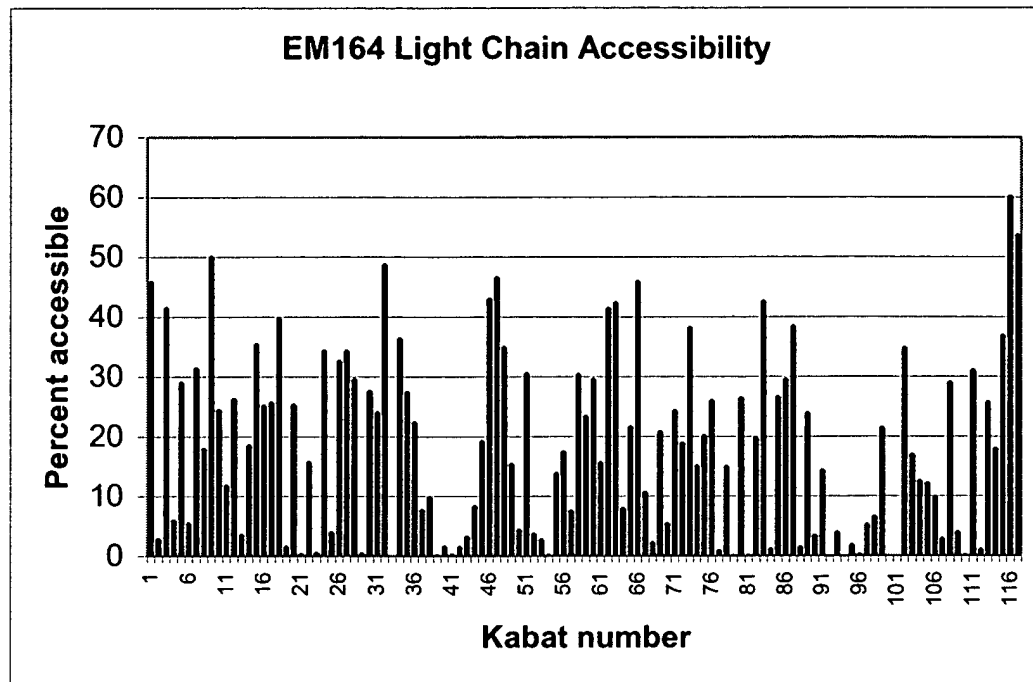
	1	10	20	30	40	50
em164 HC	QVQLQOSGAE	LVKFGASVVL	SCRASGYTFT	SYWMHNVFQR	PGQGLEWIGE	
lnqb	QVQLQOSGAE	LVKFGASVVL	SCRASGYTFT	SYWMHNVKQR	PCRGLWIGR	
lngp	QVQLQQPGAE	LVKFGASVRL	SCRASGYTFT	SYWMHNVKQR	PCRGLWIGR	
lfbi	QVQLQQPGAE	LVKFGASVLL	SCRASGYTFT	SYWMHNVKQG	PGQGLEWIGE	
lafv	QVQLQQPGSV	LVRFGASVLL	SCRASGYTFT	SSWIHNKAKQR	PGQGLEWIGE	
lyuh	QVQLQQSGAE	LVKFGASVVL	SCRASGYTFT	SYLMHNVKQR	PCRGLWIGR	
lplg	QIQLQQSGPE	LVRFGASVKI	SCRASGYTFT	DYYIHNVKQR	EGGLEWIGW	
ld5b	QVQLQQSGAE	LMKFGASVRI	SCRATGYTFS	SFWIEEVKQR	PGHGLEWIGE	
lae6	QIQLQQSGPE	LVKFGASVFI	SCRASGYTFT	DYYINNMELK	PGQGLEWIGW	
laxs	QVQLLESGAE	LMKFGASVFI	SCRATGYTFS	SFWIEEVKQR	PGHGLEWIGE	
3hfl	-VQLQQSGAE	LMKFGASVFI	SCRASGYTFS	DYWIEEVKQR	PGHGLEWIGE	
Consensus	q v Q l q q s G a e	L v k P G A S V K x	S C K A s G Y T F t	s y w x h W v K Q r	P G x G L E W I G x	

	60	70	80	90	100
em164 HC	INPNSNGRTNY	NEKFKRKATL	TVDKSSSTAY	MQLSSLTSED	SAVYYFARGR
lnqb	IDPNSGGTKY	NEKFKSKATL	TVDKPSSTAY	MQLSSLTSED	SAVYYCAR--
lngp	IDPNSGGTKY	NEKFKSKATL	TVDKPSSTAY	MQLSSLTSED	SAVYYCAR--
lfbi	IDPNSGYPNY	NEKFKGKATL	TVDKSSSTAY	MQLSSLTSED	SAVYYCAS--
lafv	IHPNSGNTNY	NEKFKGKATL	TVDTSSTAY	VDLSSLTSED	SAVYYCAR--
lyuh	IDPNNVVTKF	NEKFKSKATL	TVDKPSSTAY	MQLSSLTSED	SAVYYCAR--
lplg	IYFGSGGNTKY	NEKFKGKATL	TVDTSSTAY	MQLSSLTSED	SAVYYCAR--
ld5b	ILFGSGGTHY	NEKFKGKATF	TADKSSNTAY	MQLSSLTSED	SAVYYCARGH
lae6	IDPFGSGNTKY	NEKFKGKATL	TVDTSSTAY	MQLSSLTSED	SAVYYCAR--
laxs	ILFGSGGTHY	NEKFKGKATF	TADKSSNTAY	MQLSSLTSED	SAVYYCARGH
3hfl	ILFGSGGNTNY	HERFKGKATF	TADTSSTAY	MQLSSLTSED	SGVYYCLHGN
Consensus	I x P x s g x t x y	n E k F K g K A T l	T v D k s s s T A Y	m q L s s L T S E D	s a v Y y c a r --

	110	120	130	140	150
em164 HC	PDYVGSSKWKY	FQVWGAGTTV	TVSS		
lnqb	YDYVGSS--Y	FQVWGAGTTV	TVSS		
lngp	YDYVGSS--Y	FQVWGAGTTL	TVSS		
lfbi	LYYVGTSYGV	LDYWGAGTSV	TVSS		
lafv	-WRVYGSP--Y	FQVWGAGTTL	TVSS		
lyuh	YAYCRP----	MDYWGAGTTV	TVSS		
lplg	--GK--FA	MDYWGAGTSV	TVSS		
ld5b	S--YVF--YD	GQYWGAGTSV	TVSS		
lae6	--EKTYYYYA	MDYWGAGTSV	TVSA		
laxs	S--YVF--YD	GQYWGAGTSV	TVSS		
3hfl	-----YD	FQVWGAGTTL	TVSS		
Consensus	x x y y x x x - x x	x D y W G q G T x v	T V S S		

FIGURE 19

A.



B.

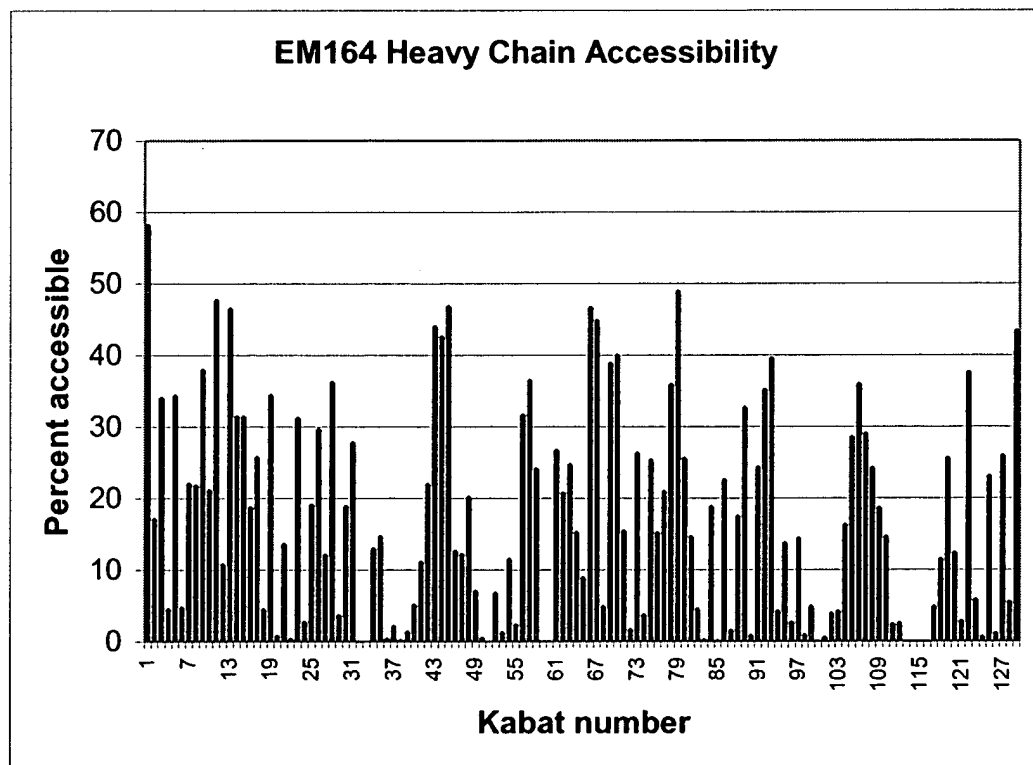


FIGURE 20

**Light Chain Variable Region Amino Acid Sequences for  
 Murine and Humanized EM164 Antibodies**

Kabat #	1	10	20	27c	35	45
muEM164	DVLMTQTPLS	LPVSLGDQAS	ISCRSSQSIV	HSNVNTYLEW	YLQKPGQSPK	
huEM164 v1.0	DVVMQTPLS	LPVSLGDPAS	ISCRSSQSIV	HSNVNTYLEW	YLQKPGQSPR	
huEM164 v1.1	DVLMTQTPLS	LPVSLGDPAS	ISCRSSQSIV	HSNVNTYLEW	YLQKPGQSPK	
huEM164 v1.2	DVLMTQTPLS	LPVSLGDPAS	ISCRSSQSIV	HSNVNTYLEW	YLQKPGQSPR	
huEM164 v1.3	DVVMQTPLS	LPVSLGDPAS	ISCRSSQSIV	HSNVNTYLEW	YLQKPGQSPK	
changes	*		*			*

Kabat #	46	55	65	75	85	95f
muEM164	LLIYKVSNR	SGVPDRFSGS	GSGTDFTLRI	SRVEAEDLGI	YYCFQGSHVP	
huEM164 v1.0	LLIYKVSNR	SGVPDRFSGS	GAGTDFTLRI	SRVEAEDLGI	YYCFQGSHVP	
huEM164 v1.1	LLIYKVSNR	SGVPDRFSGS	GAGTDFTLRI	SRVEAEDLGI	YYCFQGSHVP	
huEM164 v1.2	LLIYKVSNR	SGVPDRFSGS	GAGTDFTLRI	SRVEAEDLGI	YYCFQGSHVP	
huEM164 v1.3	LLIYKVSNR	SGVPDRFSGS	GAGTDFTLRI	SRVEAEDLGI	YYCFQGSHVP	
changes			*			

Kabat #	96	105	108
muEM164	PTFGGGTKLE	IKR	
huEM164 v1.0	PTFGGGTKLE	IKR	
huEM164 v1.1	PTFGGGTKLE	IKR	
huEM164 v1.2	PTFGGGTKLE	IKR	
huEM164 v1.3	PTFGGGTKLE	IKR	
changes			

FIGURE 21

**Heavy Chain Variable Region Amino Acid Sequences for  
 Murine and Humanized EM164 Antibodies**

Kabat #	1	10	20	30	40	50
muEM164	QVQLQQSGAE	LVKPGASVKL	SCKASGYTFT	SYWMHWVKQR	PGQGLEWIGE	
huEM164	QVQLVQSGAE	VVKPGASVKL	SCKASGYTFT	SYWMHWVKQR	PGQGLEWIGE	
changes	*	*				
Kabat #	51	59	69	79	86	96
muEM164	INPSNGRTNY	NEKFKRKATL	TVDKSSSTAY	MLSSLTSED	SAVYYFARGR	
huEM164	INPSNGRTNY	NQKFQ GKATL	TVDKSSSTAY	MLSSLTSED	SAVYYFARGR	
changes		*	**			
Kabat #	97	100f	109	113		
muEM164	PDYYGSSKWY	FDVWGAGTTV	TVSS			
huEM164	PDYYGSSKWY	FDVWGQGTTV	TVSS			
changes		*				

FIGURE 22

**huEM164 v1.0 Variable Region DNA and Amino Acid Sequences**  
Light Chain

```

1 gatgttgtgatgacccaaactccactctccctgcctgtcagtctt
1 D V V M T Q T P L S L P V S L

46 ggagatccagcctccatctcttgcagatctagtcagagcatagta
16 G D P A S I S C R S S Q S I V

91 catagtaatgtaaacacctatttagaatggtacctgcagaaacca
31 H S N V N T Y L E W Y L Q K P

136 ggccagtctccaaggctcctgatctacaaagtttccaaccgattt
46 G Q S P R L L I Y K V S N R F

181 tctggggtccagacaggttcagtggcagtggagcagggacagat
61 S G V P D R F S G S G A G T D

226 ttcacactcaggatcagcagagtggaggctgaggatctgggaatt
76 F T L R I S R V E A E D L G I

271 tattactgctttcaaggttcacatgttctccgacgttcggtgga
91 Y Y C F Q G S H V P P T F G G

316 ggcaccaaactggaaatcaaacgt
106 G T K L E I K R

```

Heavy Chain

```

1 caggtccaactgggtgcagtctggggctgaagtgggaagcctggg
1 Q V Q L V Q S G A E V V K P G

46 gcttcagtgaagctgtcctgtaaggcttctggctacaccttcacc
16 A S V K L S C K A S G Y T F T

91 agctactggatgcactgggtgaagcagaggcctggacaaggcctt
31 S Y W M H W V K Q R P G Q G L

136 gagtggattggagagattaatcctagcaacggtcgtactaactac
46 E W I G E I N P S N G R T N Y

181 aatcagaagttccagggaaggccacactgactgtagacaaatcc
61 N Q K F Q G K A T L T V D K S

226 tccagcacagcctacatgcaactcagcagcctgacatctgaggac
76 S S T A Y M Q L S S L T S E D

271 tctgcggtctattactttgcaagaggaagaccagattactacggt
91 S A V Y Y F A R G R P D Y Y G

316 agtagcaagtgggtacttctgatgtctggggccaagggaaccaggtc
106 S S K W Y F D V W G Q G T T V

361 accgtctcctca
121 T V S S

```

FIGURE 23

**huEM164 v1.1, 1.2, 1.3 Light Chain Variable Region DNA  
and Amino Acid Sequences**

v1.1

```

1 gatgttttgatgacccaaactccactctccctgcctgtcagtctt
1 D V L M T Q T P L S L P V S L

46 ggagatccagcctccatctcttgcagatctagtcagagcatagta
16 G D P A S I S C R S S Q S I V

91 catagtaatgtaaacacctatttagaatggtacctgcagaaacca
31 H S N V N T Y L E W Y L Q K P

136 ggccagtctccaaagctcctgatctacaaagtttccaaccgattt
46 G Q S P K L L I Y K V S N R F

181 tctggggtcccagacaggttcagtgccagtgaggcagggacagat
61 S G V P D R F S G S G A G T D

226 ttcacactcaggatcagcagagtgagggtgaggatctgggaatt
76 F T L R I S R V E A E D L G I

271 tattactgctttcaaggttcacatgttcctccgacgttcggtgga
91 Y Y C F Q G S H V P P T F G G

316 ggcaccaaactggaaatcaaacgt
106 G T K L E I K R

```

v1.2

```

1 gatgttttgatgacccaaactccactctccctgcctgtcagtctt
1 D V L M T Q T P L S L P V S L

46 ggagatccagcctccatctcttgcagatctagtcagagcatagta
16 G D P A S I S C R S S Q S I V

91 catagtaatgtaaacacctatttagaatggtacctgcagaaacca
31 H S N V N T Y L E W Y L Q K P

136 ggccagtctccaaaggtcctgatctacaaagtttccaaccgattt
46 G Q S P R L L I Y K V S N R F

181 tctggggtcccagacaggttcagtgccagtgaggcagggacagat
61 S G V P D R F S G S G A G T D

226 ttcacactcaggatcagcagagtgagggtgaggatctgggaatt
76 F T L R I S R V E A E D L G I

271 tattactgctttcaaggttcacatgttcctccgacgttcggtgga
91 Y Y C F Q G S H V P P T F G G

316 ggcaccaaactggaaatcaaacgt
106 G T K L E I K R

```

(FIGURE 23, CONT.)

v1.3

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1 gatgttgtgatgacccaaactccactctccctgcctgtcagtcctt
1 D V V M T Q T P L S L P V S L

46 ggagatccagcctccatctcttgcagatctagtcagagcatagta
16 G D P A S I S C R S S Q S I V

91 catagtaatgtaaaccacctaatttagaatggtacctgcagaaacca
31 H S N V N T Y L E W Y L Q K P

136 ggccagtctccaaagctcctgatctacaaagtttccaaccgattt
46 G Q S P K L L I Y K V S N R F

181 tctgggggtcccagacagggttcagtggtgagcagggacagat
61 S G V P D R F S G S G A G T D

226 ttcacactcaggatcagcagagtgagggtgaggatctgggaatt
76 F T L R I S R V E A E D L G I

271 tattactgctttcaagggttcacatgttcctccgacgttcggtgga
91 Y Y C F Q G S H V P P T F G G

316 ggcaccaaactggaaatcaaacgt
106 G T K L E I K R
```



**FIGURE 24**  
**Comparison of inhibition of IGF-I-stimulated growth and survival of MCF-7 cells by humanized EM164 v1.0 antibody (6-25 µg/mL) vs murine EM164 antibody (5-10 µg/mL)**

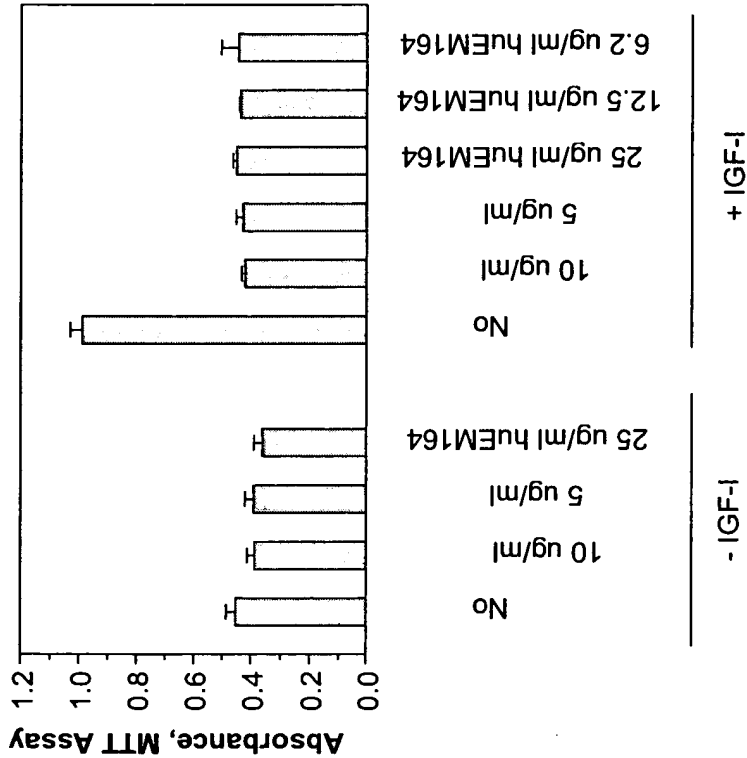


FIGURE 25

# Cell cycle arrest of MCF-7 cells by EM164 antibody

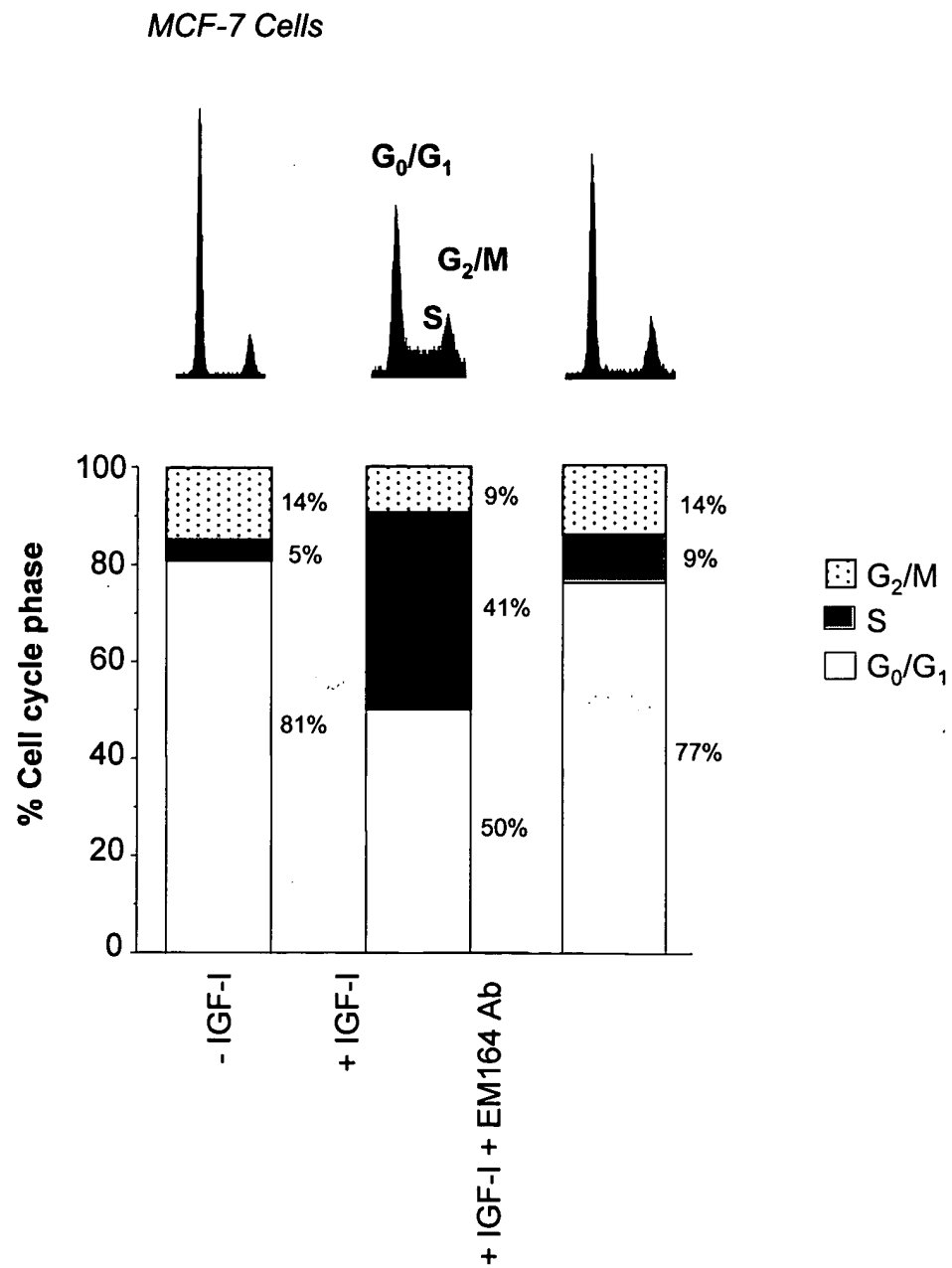


FIGURE 26

**Induction of apoptosis in NCI-H838 lung cancer cells by EM164 antibody  
(measured from the cleavage of cytokeratin CK18 protein by caspase)**

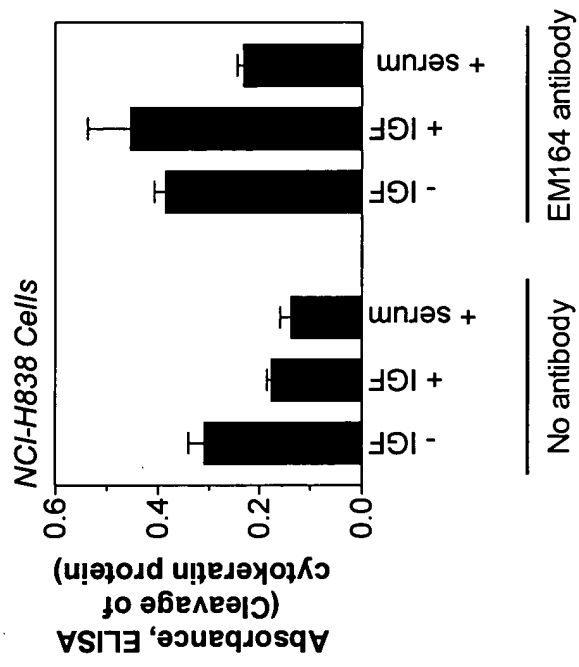


FIGURE 27

Suppression of growth of BxPC-3 human pancreatic cancer xenografts in mice by EM164 antibody treatment as a single agent or in combination with gemcitabine

